

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

United States Patent and Trademark
Office
Washington, D.C.

in its capacity as elected Office

Date of mailing:

10 January 1994 (10.01.94)

International application No.:

PCT/SE93/00375

Applicant's or agent's file reference:

25364-28723-Fa

International filing date:

28 April 1993 (28.04.93)

Priority date:

28 April 1992 (28.04.92)

Applicant:

BJÖRCK, Lars et al

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

15 November 1993 (15.11.93)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was



was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer:

I. Hours

Telephone No.: (41-22) 730.91.11

PATENT COOPERATION TREATY

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**NOTIFICATION CONCERNING
DOCUMENT TRANSMITTED**

From the INTERNATIONAL BUREAU

To:

**United States Patent and Trademark
Office
Washington, D.C.**

in its capacity as elected Office

Date of mailing:

06 June 1994 (06.06.94)

International application No.:

PCT/SE93/00375

International filing date:

28 April 1993 (28.04.93)

Applicant:

HIGHTECH RECEPTOR AB et al

The International Bureau transmits herewith the following documents and number thereof:

_____ copy of the international preliminary examination report and annexes (Article 36(3)(a))

**The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland**

Facsimile No.: (41-22) 740.14.35

Authorised officer:

C. Carrié

Telephone N .: (41-22) 730.91.11

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

To:

BERG, S., A.
H. Albihns Patentbyrå AB
Box 3137
S-103 62 Stockholm
SUEDEDate of mailing 15 September 1994
(day/month/year) (15.09.94)Applicant's or agent's file reference
25364-28723-Fa

IMPORTANT NOTIFICATION

International application No.
PCT/SE93/00375International filing date
(day/month/year) 28 April 1993 (28.04.93)

1. The following indications appeared on record concerning:

☒ the applicant ☐ the inventor ☐ the agent ☐ the common representative

Name and Address

HIGHECH RECEPTOR AB
c/o Active
Skeppsbron 2
S-211 20 Malmö
Sweden

State of Nationality

State of Residence

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☒ the address ☐ the nationality ☐ the residence

Name and Address

c/o Active i Malmö AB
Stora Nygatan 61
S-211 37 Malmö
Sweden

State of Nationality

State of Residence

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned
☐ the International Searching Authority ☒ the elected Offices concerned
☐ the International Preliminary Examining Authority ☐ other:The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

I. Hours

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 25364-28723-Fa	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/ SE 93/ 00375	International filing date (day/month/year) 28/04/1993	Priority date (day/month/year) 28/04/1992
International Patent Classification (IPC) or national classification and IPC C07K13/00		
Applicant HighTech Receptor AB et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 6 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings amended during international preliminary examination and/or containing rectifications made before this Authority.

These annexes consists of a total of 7 sheets.

3. This report contains indications and corresponding pages relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 15/11/1993	Date of completion of this report 01.06.94
Name and mailing address of the IPEA/  European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer K. Heckl 

I. Basis of the report

1. This report has been drawn up on the basis of:

☐ the international application as originally filed.

☒ the description, pages 1-40 _____, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____.

☒ the claims, No. _____, as originally filed,
No. _____, as amended under Article 19,
No. _____, filed with the demand,
No. 1-13 _____, filed with the letter of 3.5.94____,
No. _____, filed with the letter of _____.

☒ the drawings, sheets/fig 1/18-18/18 _____, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of: pages: 41-48 (claims 1-14) _____
sheets of drawings/figures No.: _____.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed:

4. Additional observations, if necessary:

In the file of the IPEA the originally filed documents were not available. Accordingly, it could not be examined if the published application fully corresponds to the documents originally filed.

In consequence, the International Preliminary Examination has been carried out on the basis of the International Applica-

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Intern. application No.

PCT/SE93/00375

tion published under the PCT (WO 93/22342).

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Intern. application No.

PCT/SE93/00375

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1 (partially), 2-10, 11-13 (partially)_____	YES
	Claims 1 (partially), 11-13 (partially)_____	NO
Inventive Step (IS)	Claims 1 (partially), 2-9, 10-13 (partially)_____	YES
	Claims 10 (partially)_____	NO
Industrial Applicability (IA)	Claims 1-13_____	YES
	Claims _____	NO

2. CITATIONS AND EXPLANATIONS

1. The particular protein L variant of the present application as identified by the sequences of claims 1 and 2 is novel and comprises an inventive step (Art.33(2) and (3) PCT).
- 1.1 EP-A2-0 255 479 (D1) discloses the existence of a particular protein L variant derived from P.magnus 312, however, without indicating its primary structure.
- 1.2 It becomes evident by comparing the particular sequence fragment of Infection and Immunity 58/5, 1990, 1217-1222 (D2), Fig.5, with its corresponding part of the sequence of claim 1 that the present application discloses a protein L variant which is different to that of D2.
- 1.3 Said finding is considered surprising as the cited prior art does not allow to assume or conclude the existence of a further protein L variant of P.magnus in an obvious manner.

Moreover, the variants of D2 and the present application have been isolated from the same strain, i.e. P.magnus 312, which fact allows to conclude that the present application seems to disclose a further allelic protein L variant. In the absence of any hint or evidence to the existence of a further (allelic) protein L variant of P.magnus 312, said finding allows to acknowledge an inventive step.

- 1.4 The same applies to the "subfragments and multiples or mixtures of the B1-B5 domains having the same binding properties" of claim 1, to the particular hybrid proteins of claims 3-7 comprising one or more of the B1-B5 domains according to claim 1, and to the plasmids and hosts of claims 8 and 9, too.
- 1.5 In addition, the subject matter of claims 10-13, as far as referring to the novel and inventive subject matter as identified above, meets the requirements of Art.33(2) and (3) PCT, too.
2. However, claims 1 and 11-13 also comprise subject matter which does not seem to be novel (Art.33(2) PCT).
- 2.1 The "variants having the same binding properties" of claim 1 - without precisely defining said variants - fall under the scope of D1, page 2 and claims 1 and 2, and of D2, abstract, materials and methods, "purification of protein L" and Fig.1, thus contravening Art.33(2) PCT.

Indeed, both the proteins L of D1 and D2 and that of the present application share the same source, have identical molecular weights and the same binding properties. Hence, D1 and D2 undoubtedly represent particular protein L variants. Accordingly, the "variants" of claim 1 include the particular variants of D1 or D2, as well.

2.2 In consequence, claims 11-13, referring to said protein L variants, as well, and their use in kits and pharmaceutical compositions, comprise known subject matter (see inter alia D1, claims 10 and 11).

3. The subject matter of claim 10, as far as referred back to the "variants" objected to under Art.33(2) PCT (see above, item 2.1) lacks an inventive step (Art.33(3) PCT).

The skilled person is aware of the appropriate technical teaching which allows to clone and express the full length cDNA encoding the protein L variant of D2 with reasonable expectation of success.

4. The priority documents pertaining to the present application were not available at the time of establishing this written opinion. Hence, it is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is not correct, the document J.Biol.Chem.267/18, 1992, 12820-12815, cited in the international search report could become relevant to assess whether claims satisfy the criteria set forth in Article 33(1) PCT.

Claims

1. Protein L having the ability to bind to the light chains of immunoglobulins, characterized in that the protein L has the following amino acid sequence:

— B1

Ala	Val	Glu	Asn	Lys	Glu	Glu	Thr	Pro	Glu	Thr	Pro	Glu	Thr	Asp	Ser	1	5	10	15
Glu	Glu	Glu	Val	Thr	Ile	Lys	Ala	Asn	Leu	Ile	Phe	Ala	Asn	Gly	Ser	20	25	30	
Thr	Gln	Thr	Ala	Glu	Phe	Lys	Gly	Thr	Phe	Glu	Lys	Ala	Thr	Ser	Glu	35	40	45	
Ala	Tyr	Ala	Tyr	Ala	Asp	Thr	Leu	Lys	Lys	Asp	Asn	Gly	Glu	Tyr	Thr	50	55	60	
Val	Asp	Val	Ala	Asp	Lys	Gly	Tyr	Thr	Leu	Asn	Ile	Lys	Phe	Ala	Gly	65	70	75	80
Lys	Glu	Lys	Thr	Pro	Glu	Glu	Pro	Lys	Glu	Glu	Val	Thr	Ile	Lys	Ala	85	90	95	
Asn	Leu	Ile	Tyr	Ala	Asp	Gly	Lys	Thr	Gln	Thr	Ala	Glu	Phe	Lys	Gly	100	105	110	
Thr	Phe	Glu	Glu	Ala	Thr	Ala	Glu	Ala	Tyr	Arg	Tyr	Ala	Asp	Ala	Leu	115	120	125	
Lys	Lys	Asp	Asn	Gly	Glu	Tyr	Thr	Val	Asp	Val	Ala	Asp	Lys	Gly	Tyr	130	135	140	
Thr	Leu	Asn	Ile	Lys	Phe	Ala	Gly	Lys	Glu	Lys	Thr	Pro	Glu	Glu	Pro	145	150	155	160
Lys	Glu	Glu	Val	Thr	Ile	Lys	Ala	Asn	Leu	Ile	Tyr	Ala	Asp	Gly	Lys	165	170	175	
Thr	Gln	Thr	Ala	Glu	Phe	Lys	Gly	Thr	Phe	Glu	Glu	Ala	Thr	Ala	Glu	180	185	190	
Ala	Tyr	Arg	Tyr	Ala	Asp	Leu	Leu	Ala	Lys	Glu	Asn	Gly	Lys	Tyr	Thr	195	200	205	
Val	Asp	Val	Ala	Asp	Lys	Gly	Tyr	Thr	Leu	Asn	Ile	Lys	Phe	Ala	Gly	210	215	220	

— B3

—— B4

Lys Glu Lys Thr Pro Glu Glu Pro Lys Glu Glu Val Thr Ile Lys Ala
225 230 235 240

5 Asn Leu Ile Tyr Ala Asp Gly Lys Thr Gln Thr Ala Glu Phe Lys Gly
245 250 255

Thr Phe Ala Glu Ala Thr Ala Glu Ala Tyr Arg Tyr Ala Asp Leu Leu
260 265 270

10 Ala Lys Glu Asn Gly Lys Tyr Thr Ala Asp Leu Glu Asp Gly Gly Tyr
275 280 — B5 285

Thr Ile Asn Ile Arg Phe Ala Gly Lys Lys Val Asp Glu Lys Pro Glu
290 295 300

Glu

15

and variants, subfragments, multiples or mixtures of the domains B1-B5 having the same binding properties.

20 2. DNA-sequence, characterized in that it codes for the protein according to Claim 1 and has the following nucleotide sequence:

	GCG GTA GAA AAT AAA GAA GAA ACA CCA GAA ACA CCA GAA ACT GAT TCA	25
25	GAA GAA GAA GTA ACA ATC AAA GCT AAC CTA ATC TTT GCA AAT GGA AGC	96
	ACA CAA ACT GCA GAA TTC AAA GGA ACA TTT GAA AAA GCA ACA TCA GAA	144
	GCT TAT GCG TAT GCA GAT ACT TTG AAG AAA GAC AAT GGA GAA TAT ACT	192
30	GTA GAT GTT GCA GAT AAA GGT TAT ACT TTA AAT ATT AAA TTT GCT GGA	240
	AAA GAA AAA ACA GCA GAA GAA CCA AAA GAA GAA GTT ACT ATT AAA GCA	288
	AAC TTA ATC TAT GCA GAT GGA AAA ACA CAA ACA GCA GAA TTC AAA GGA	336
	ACA TTT GAA GAA GCA ACA GCA GAA GCA TAC AGA TAT GCA GAT GCA TTA	384
35	AAG AAG GAC AAT GGA GAA TAT ACA GTA GAC GTT GCA GAT AAA GGT TAT	432
	ACT TTA AAT ATT AAA TTT GCT GGA AAA GAA AAA ACA CCA GAA GAA CCA	480
	AAA GAA GAA GTT ACT ATT AAA GCA AAC TTA ATC TAT GCA GAT GGA AAA	528

ACA CAA ACA GCA GAA TTC AAA GGA ACA TTT GAA GAA GCA ACA GCA GAA 576
 5 GCA TAC AGA TAT GGT GAC TTA TTA GCA AAA GAA AAT GGT AAA TAT ACA 624
 GTA GAC GTT GCA GAT AAA GGT TAT ACT TTA AAT ATT AAA TTT GCT GGA 672
 AAA GAA AAA ACA CCA GAA GAA CCA AAA GAA GAA GTT ACT ATT AAA GCA 720
 AAC TTA ATC TAT GCA GAT GGA AAA ACT CAA ACA GCA GAG TTC AAA GGA 768
 10 ACA TTT GCA GAA GCA ACA GCA GAA GCA TAC AGA TAC GCT GAC TTA TTA 816
 GCA AAA GAA AAT GGT AAA TAT ACA GCA GAC TTA GAA GAT GGT GGA TAC 864
 ACT ATT AAT ATT AGA TTT GCA GGT AAG AAA GTT GAC GAA AAA CCA GAA 912
 15 GAA TAATAA 921

3. A hybrid protein, characterized in
 that it includes one or more of the B1-B5-domains ac-
 20 cording to Claim 1 which bind to the light chains in
 immunoglobulins of all classes, and domains which bind
 to heavy chains in immunoglobulin G.
4. A hybrid protein according to Claim 3, char-
 25 acterized in that the domains which bind to
 heavy chains in immunoglobulin G are chosen from among
 the C1- and C2-domains in protein G or from among any
 other functionally similar proteins which bind to heavy
 chains in immunoglobulin G, and variants, subfragments,
 30 multiples or mixtures thereof having the same binding
 properties.
5. A hybrid protein according to Claim 4, char-
 acterized in that the hybrid protein has the
 35 following amino acid sequence:

	Ala	Val	Glu	Asn	Lys	Glu	Glu	Thr	Pro	Glu	Thr	Pro	Glu	Thr	Asp	Ser	
					5					10					15		
5	Glu	Glu	Glu	Val	Thr	Ile	Lys	Ala	Asn	Leu	Ile	Phe	Ala	Asn	Gly	Ser	
				20					25						30		
	Thr	Gln	Thr	Ala	Glu	Phe	Lys	Gly	Thr	Phe	Glu	Lys	Ala	Thr	Ser	Glu	
				35				40						45			
10	Ala	Tyr	Ala	Tyr	Ala	Asp	Thr	Leu	Lys	Lys	Asp	Asn	Gly	Glu	Tyr	Thr	
		50					55						60				
	Val	Asp	Val	Ala	Asp	Lys	Gly	Tyr	Thr	Leu	Asn	Ile	Lys	Phe	Ala	Gly	
		65				70					75					80	
	Lys	Glu	Lys	Thr	Pro	Glu	Glu	Pro	Lys	Glu	Glu	Val	Thr	Ile	Lys	Ala	
15					85					90						95	
	Asn	Leu	Ile	Tyr	Ala	Asp	Gly	Lys	Thr	Gln	Thr	Ala	Glu	Phe	Lys	Gly	
				100					105					110			
	Thr	Phe	Glu	Glu	Ala	Thr	Ala	Glu	Ala	Tyr	Arg	Tyr	Ala	Asp	Ala	Leu	
			115					120					125				
20	Lys	Lys	Asp	Asn	Gly	Glu	Tyr	Thr	Val	Asp	Val	Ala	Asp	Lys	Gly	Tyr	
			130				135					140					
	Thr	Leu	Asn	Ile	Lys	Phe	Ala	Gly	Lys	Glu	Lys	Thr	Pro	Glu	Glu	Pro	
		145				150					155					160	
25	Lys	Glu	Glu	Val	Thr	Ile	Lys	Ala	Asn	Leu	Ile	Tyr	Ala	Asp	Gly	Lys	
				165						170					175		
	Thr	Gln	Thr	Ala	Glu	Phe	Lys	Gly	Thr	Phe	Glu	Glu	Ala	Thr	Ala	Glu	
				180					185					190			
	Ala	Tyr	Arg	Tyr	Ala	Asp	Leu	Leu	Ala	Lys	Glu	Asn	Gly	Lys	Tyr	Thr	
30			195					200					205				
	Val	Asp	Val	Ala	Asp	Lys	Gly	Tyr	Thr	Leu	Asn	Ile	Lys	Phe	Ala	Gly	
		210					215					220					
	Lys	Glu	Lys	Thr	Pro	Glu	Glu	Pro	Lys	Glu	Glu	Val	Thr	Ile	Lys	Ala	
		225				230					235					240	
35	Asn	Leu	Ile	Tyr	Ala	Asp	Gly	Lys	Thr	Gln	Thr	Ala	Glu	Phe	Lys	Gly	
					245					250					255		

45

Thr Phe Ala Glu Ala Thr Ala Glu Ala Tyr Arg Tyr Ala Asp Leu Leu
 260 265 270
 5 Ala Lys Glu Asn Gly Lys Tyr Thr Ala Asp Leu Glu Asp Gly Gly Tyr
 275 280 285
 Thr Ile Asn Ile Arg Phe Ala Gly Lys Lys Val Asp Glu Lys Pro Glu
 290 295 300
 10 Glu Pro Met Asp Thr Tyr Lys Leu Ile Leu Asn Gly Lys Thr Leu Lys
 305 310 315 320
 Gly Glu Thr Thr Thr Glu Ala Val Asp Ala Ala Thr Ala Glu Lys Val
 325 330 335
 15 Phe Lys Gln Tyr Ala Asn Asp Asn Gly Val Asp Gly Glu Trp Thr Tyr
 340 345 350
 Asp Asp Ala Thr Lys Thr Phe Thr Val Thr Glu Lys Pro Glu Val Ile
 355 360 365
 Asp Ala Ser Glu Leu Thr Pro Ala Val Thr Thr Tyr Lys Leu Val Ile
 370 375 380
 20 Asn Gly Lys Thr Leu Lys Gly Glu Thr Thr Thr Lys Ala Val Asp Ala
 385 390 395 400
 Glu Thr Ala Glu Lys Ala Phe Lys Gln Tyr Ala Asn Asp Asn Gly Val
 405 410 415
 25 Asp Gly Val Trp Thr Tyr Asp Asp Ala Thr Lys Thr Phe Thr Val Thr
 420 425 430

Glu Met

30 and variants, subfragments, multiples or mixtures of the
 domains B1-B5 having the same binding properties.

6. DNA-sequence, characterized in that
 it codes for a protein according to Claim 5 and has the
 35 following nucleotide sequence:

AMENDED SHEET

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	GCG	GTA	GAA	AAT	AAA	GAA	GAA	ACA	CCA	GAA	ACA	CCA	GAA	ACT	GAT	TCA	28
	GAA	GAA	GAA	GTA	ACA	ATC	AAA	GCT	AAC	CTA	ATC	TTT	GCA	AAT	GGA	AGC	96
	ACA	CAA	ACT	GCA	GAA	TTC	AAA	GGA	ACA	TTT	GAA	AAA	GCA	ACA	TCA	GAA	124
	GCT	TAT	GCG	TAT	GCA	GAT	ACT	TGG	AAG	AAA	GAC	AAT	GGA	GAA	TAT	ACT	192
5	GTA	GAT	GTT	GCA	GAT	AAA	GGT	TAT	ACT	TTA	AAT	ATT	AAA	TTT	GCT	GGA	240
	AAA	GAA	AAA	ACA	CCA	GAA	GAA	CCA	AAA	GAA	GAA	GTT	ACT	ATT	AAA	GCA	288
	AAC	TTA	ATC	TAT	GCA	GAT	GGA	AAA	ACA	CAA	ACA	GCA	GAA	TTC	AAA	GGA	336
10	ACA	TTT	GAA	GAA	GCA	ACA	GCA	GAA	GCA	TAC	AGA	TAT	GCA	GAT	GCA	TTA	384
	AAG	AAG	GAC	AAT	GGA	GAA	TAT	ACA	GTA	GAC	GTT	GCA	GAT	AAA	GGT	TAT	432
	ACT	TTA	AAT	ATT	AAA	TTT	GCT	GGA	AAA	GAA	AAA	ACA	CCA	GAA	GAA	CCA	480
	AAA	GAA	GAA	GTT	ACT	ATT	AAA	GCA	AAC	TTA	ATC	TAT	GCA	GAT	GGA	AAA	528
15	ACA	CAA	ACA	GCA	GAA	TTC	AAA	GGA	ACA	TTT	GAA	GAA	GCA	ACA	GCA	GAA	576
	GCA	TAC	AGA	TAT	GCT	GAC	TTA	TTA	GCA	AAA	GAA	AAT	GGT	AAA	TAT	ACA	624
	GTA	GAC	GTT	GCA	GAT	AAA	GGT	TAT	ACT	TTA	AAT	ATT	AAA	TTT	GCT	GGA	672
20	AAA	GAA	AAA	ACA	CCA	GAA	GAA	CCA	AAA	GAA	GAA	GTT	ACT	ATT	AAA	GCA	720
	AAC	TTA	ATC	TAT	GCA	GAT	GGA	AAA	ACT	CAA	ACA	GCA	GAG	TTC	AAA	GGA	768
	ACA	TTT	GCA	GAA	GCA	ACA	GCA	GAA	GCA	TAC	AGA	TAC	GCT	GAC	TTA	TTA	816
	GCA	AAA	GAA	AAT	GGT	AAA	TAT	ACA	GCA	GAC	TTA	GAA	GAT	GGT	GGA	TAC	864
25	ACT	ATT	AAT	ATT	AGA	TTT	GCA	GGT	AAG	AAA	GTT	GAC	GAA	AAA	CCA	GAA	912
	GAA	CCC	ATG	GAC	ACT	TAC	AAA	TTA	ATC	CTT	AAT	GGT	AAA	ACA	TTG	AAA	960
	GCG	GAA	ACA	ACT	ACT	GAA	GCT	GTT	GAT	GCT	GCT	ACT	GCA	GAA	AAA	GTC	1008
30	TTC	AAA	CAA	TAC	GCT	AAC	GAC	AAC	GGT	GTT	GAC	GGT	GAA	TGG	ACT	TAC	1056
	GAC	GAT	GCG	ACT	AAG	ACC	TTT	ACA	GTT	ACT	GAA	AAA	CCA	GAA	GTG	ATC	1104
	GAT	GCG	TCT	GAA	TTA	ACA	CCA	GCC	GTG	ACA	ACT	TAC	AAA	CTT	GTT	ATT	1152
	AAT	GGT	AAA	ACA	TTG	AAA	GCG	GAA	ACA	ACT	ACT	AAA	GCA	GTA	GAC	GCA	1200
35	GAA	ACT	GCA	GAA	AAA	GCC	TTC	AAA	CAA	TAC	GCT	AAC	GAC	AAC	GGT	GTT	1248
	GAT	GGT	GTT	TGG	ACT	TAT	GAT	GAT	GCG	ACT	AAG	ACC	TTT	ACG	GTA	ACT	1296
	GAA	ATG	TAATAA														1308

AMENDED SHEET

7. DNA-sequence, characterized in that it codes for a protein according to Claims 3, 4 and 5.

5 8. A plasmid vector, characterized in that it includes a DNA-sequence according to any one of Claims 2 and 6-8, preferably the vector pHDLG or pHDL according to Fig. 3 or 4.

10 9. A host cell, characterized in that it is transformed with the hybrid plasmid according to Claim 9, in particular a host which belongs to the species E. coli, particularly E. coli LE392, or Bacillus subtilis, Saccaromyces cerevisiae, preferably Id. Ref. DSSM E. coli LE392 pHDL and E. coli LE392/pHDLG respectively.

15 10. A method for producing a protein according to Claims 1 and 3-5, characterized by cultivating a host cell according to Claim 10 under suitable conditions; accumulating the protein in the culture or lysing the cells and extracting the protein therefrom.

20 11. A reagent kit for binding, separating and identifying immunoglobulins, characterized in that it includes a protein according to any one of Claims 1 and 3-5.

25 12. A composition, characterized in that it includes a protein according to any one of Claims 1 and 3-5, and optionally additives or carriers.

30 13. A pharmaceutical composition, characterized in that it includes a protein according to any one of Claims 1 and 3-5, and optionally a pharmaceutically acceptable carrier or extender.

55 Rec'd PCT/PTO 26 OCT 1994

08/325278

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application" *Doc*Applicant's or agent's file reference
(if desired) (12 characters maximum) 25364-28723-Fa

Box No. I TITLE OF INVENTION

PROTEIN L AND HYBRID PROTEINS THEREOF

Box No. II APPLICANT

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

HighTech Receptor AB
c/o Active
Skeppsbron 2
S-211 20 MALMÖ
Sweden

☐ This person is also inventor.

Telephone No.

Facsimile No.

Teleprinter No.

State (i.e. country) of nationality:
SwedenState (i.e. country) of residence:
SwedenThis person is applicant
for the purposes of:☐all designated
States☒all designated States except
the United States of America☐the United States
of America only☐the States indicated in
the Supplemental Box

Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

Björck, Lars
Kornvägen 40
S-240 17 SÖDRA SANDBY
Sweden

This person is:

☐ applicant only☒ applicant and inventor☐ inventor only (If this check-box
is marked, do not fill in below.)State (i.e. country) of nationality:
SwedenState (i.e. country) of residence:
SwedenThis person is applicant
for the purposes of:☐all designated
States☐all designated States except
the United States of America☒the United States
of America only☐the States indicated in
the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

Sjöbring, Ulf
Lilla Sigridsgatan 1
S-223 50 LUND
Sweden

This person is:

☐ applicant only☒ applicant and inventor☐ inventor only (If this check-box
is marked, do not fill in below.)State (i.e. country) of nationality:
SwedenState (i.e. country) of residence:
SwedenThis person is applicant
for the purposes of:☐all designated
States☐all designated States except
the United States of America☒the United States
of America only☐the States indicated in
the Supplemental Box☐ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE	
The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: <input checked="" type="checkbox"/> agent <input type="checkbox"/> common representative	
Name and address: <i>(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)</i> H. ... Eos: S A ... L-O Kierkegaard, S Lagman	Telephone No. +46 8 796 62 00
	Fascimile No. +46 8 101923
	Teleprinter No. 11942 ALBIHNS S
<input type="checkbox"/> Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.	

Box No.V DESIGNATION OF STATES	
The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):	
Regional Patent	
<input checked="" type="checkbox"/> EP European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, DE Germany, DK Denmark, ES Spain, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT	
<input type="checkbox"/> OA OAPI Patent: Benin, Burkina Faso, Cameroon, Central African Republic, Chad, Congo, Côte d'Ivoire, Gabon, Guinea, Mali, Mauritania, Senegal, Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)	
National Patent (if other kind of protection or treatment desired, specify on dotted line):	
<input type="checkbox"/> AT Austria <input type="checkbox"/> AU Australia <input type="checkbox"/> BB Barbados <input type="checkbox"/> BG Bulgaria <input type="checkbox"/> BR Brazil <input type="checkbox"/> CA Canada <input type="checkbox"/> CH and LI Switzerland and Liechtenstein <input type="checkbox"/> CZ Czech Republic <input type="checkbox"/> DE Germany <input type="checkbox"/> DK Denmark <input type="checkbox"/> ES Spain <input type="checkbox"/> FI Finland <input type="checkbox"/> GB United Kingdom <input type="checkbox"/> HU Hungary <input checked="" type="checkbox"/> JP Japan <input type="checkbox"/> KP Democratic People's Republic of Korea <input type="checkbox"/> KR Republic of Korea <input type="checkbox"/> LK Sri Lanka <input type="checkbox"/> LU Luxembourg	<input type="checkbox"/> MG Madagascar <input type="checkbox"/> MN Mongolia <input type="checkbox"/> MW Malawi <input type="checkbox"/> NL Netherlands <input type="checkbox"/> NO Norway <input type="checkbox"/> NZ New Zealand <input type="checkbox"/> PL Poland <input type="checkbox"/> PT Portugal <input type="checkbox"/> RO Romania <input type="checkbox"/> RU Russian Federation <input type="checkbox"/> SD Sudan <input type="checkbox"/> SE Sweden <input type="checkbox"/> SK Slovak Republic <input type="checkbox"/> UA Ukraine <input checked="" type="checkbox"/> US United States of America Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet: <input type="checkbox"/> <input type="checkbox"/>

In addition to the designations made above, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except the designation(s) of _____.

The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.

Box No. VI PRIORITY CLAIM		Further priority claims are indicated in the Supplemental Box <input type="checkbox"/>	
The priority of the following earlier application(s) is hereby claimed:			
Country (in which, or for which, the application was filed)	Filing Date (day/month/year)	Application No.	Office of filing (only for regional or international application)
item (1) Sweden	28.04.92 28 April 1992	9201331-7	
item (2)			
item (3)			
Mark the following check-box if the certified copy of the earlier application is to be issued by the Office which for the purposes of the present international application is the receiving Office (a fee may be required): <input type="checkbox"/> The receiving Office is hereby requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s): _____			
Box No. VII EARLIER SEARCH			
Fill in where a search (international, international-type or other) by the International Searching Authority has already been carried out or requested and the Authority is now requested to base the international search, to the extent possible, on the results of that earlier search. Identify such search or request either by reference to the relevant application (or the translation thereof) or by reference to the search request:			
Country (or regional Office):	Date (day/month/year):	Number:	
Sweden	10 December 1992	SE92/00284	
Box No. VIII CHECK LIST			
This international application contains the following number of sheets: 1. request : 3 sheets 2. description : 34 sheets 3. claims : 9 sheets 4. abstract : 1 sheets 5. drawings : 21 sheets Total : 68 sheets		This international application is accompanied by the item(s) marked below: 1. <input type="checkbox"/> separate signed power of attorney 2. <input type="checkbox"/> copy of general power of attorney 3. <input type="checkbox"/> statement explaining lack of signature 4. <input checked="" type="checkbox"/> priority document(s) identified in Box No. VI as item(s): 5. <input checked="" type="checkbox"/> fee calculation sheet 6. <input type="checkbox"/> separate indications concerning deposited microorganisms 7. <input type="checkbox"/> nucleotide and/or amino acid sequence listing (diskette) 8. <input checked="" type="checkbox"/> other (specify): SE92/00284	
Figure No. 3 of the drawings (if any) should accompany the abstract when it is published.			
Box No. IX SIGNATURE OF APPLICANT OR AGENT			
Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request). Hélène Fagerlin			

For receiving Office use only	
1. Date of actual receipt of the purported international application: 3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application: 4. Date of timely receipt of the required corrections under PCT Article 11(2): 5. International Searching Authority specified by the applicant: ISA/	2. Drawings: <input type="checkbox"/> received: <input type="checkbox"/> not received: 6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid

For International Bureau use only
Date of receipt of the record copy by the International Bureau:

BUDAPEST TREATY ON THE INTERNATIONAL
RECOGNITION OF THE DEPOSIT OF MICROORGANISMS
FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

HighTech Receptor AB
Malmö Börshus
S-211 20 Malmö

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT
issued pursuant to Rule 7.1 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR LE392/pHDL	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 7054
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNATION	
The microorganism identified under I. above was accompanied by: () a scientific description (X) a proposed taxonomic designation (Mark with a cross where applicable)	
III. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts this microorganism identified under I. above, which was received by it on 1992-04-28 (Date of original deposit) ¹	
IV. RECEIPT OF REQUEST FOR CONVERSION	
The microorganism identified under I above was received by this International Depositary Authority on (date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on (date of receipt of request for conversion).	
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Adress: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s): <i>U. Weisk</i> Date: 1992-05-04

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired.

BUDAPEST TREATY ON THE INTERNATIONAL
COGNITION OF THE DEPOSIT OF MICROORGANISMS
FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

HighTech Receptor AB
Malmö Börshus
S-211 20 Malmö

VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. DEPOSITOR	II. IDENTIFICATION OF THE MICROORGANISM
Name: HighTech Receptor AB Malmö Börshus Address: S-211 20 Malmö	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 7054 Date of the deposit or of the transfer ¹ : 1992-04-28
III. VIABILITY STATEMENT	
The viability of the microorganism identified under II above was tested on 1992-04-28 ² On that date, the said microorganism was (X) ³ viable () ³ no longer viable	
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED⁴	
IV. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s): <i>U. Weiths</i> Date: 1992-05-04

¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).

² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

BUDAPEST TREATY ON THE INTERNATIONAL
RECOGNITION OF THE DEPOSIT OF MICROORGANISMS
FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

HighTech Receptor AB
Malmö Börshus
S-211 20 Malmö

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT
issued pursuant to Rule 7.1 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR LE392/pHDLG	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 7055
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNATION	
The microorganism identified under I. above was accompanied by: () a scientific description (X) a proposed taxonomic designation (Mark with a cross where applicable)	
III. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts this microorganism identified under I. above, which was received by it on 1992-04-28 (Date of original deposit) ¹	
IV. RECEIPT OF REQUEST FOR CONVERSION	
The microorganism identified under I above was received by this International Depositary Authority on (date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on (date of receipt of request for conversion).	
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Adress: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s): <i>U. Weis</i> Date: 1992-05-04

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired.

BUDAPEST TREATY ON THE INTERNATIONAL
RECOGNITION OF THE DEPOSIT OF MICROORGANISMS
FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM



HighTech Receptor AB
Malmö Börshus
S-211 20 Malmö

VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITORY AUTHORITY
identified at the bottom of this page

I. DEPOSITOR	II. IDENTIFICATION OF THE MICROORGANISM
Name: HighTech Receptor AB Malmö Börshus Address: S-211 20 Malmö	Accession number given by the INTERNATIONAL DEPOSITORY AUTHORITY: DSM 7055 Date of the deposit or of the transfer ¹ : 1992-04-28
III. VIABILITY STATEMENT	
The viability of the microorganism identified under II above was tested on 1992-04-28 ² On that date, the said microorganism was (X) ³ viable () ³ no longer viable	
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED⁴	
IV. INTERNATIONAL DEPOSITORY AUTHORITY	
Name: DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depository Authority or of authorized official(s): <i>U. Weiler</i> Date: 1992-05-04

¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).

² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 93/00375

A. CLASSIFICATION OF SUBJECT MATTER

IPC5: C07K 13/00, C12N 15/31, C12N 15/62, A61K 37/02, C07K 3/18
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC5: C07K, C12N, A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP, A2, 0255497 (HIGHECH RECEPTOR AB), 3 February 1988 (03.02.88)	1-2,8-14
Y	WO, A1, 8705631 (PHARMACIA AB), 24 Sept 1987 (24.09.87), see especially claim 9	3-14
P,X	The Journal of Biological Chemistry, Volume 267, No 18, 1992, William Kastern et al, "Structure of Peptostreptococcal Protein L and Identification of a Repeated Immunoglobulin Light Chain-binding Domain", pp. 12820-12825	1-2,8-14

☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "B" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

21 July 1993

Name and mailing address of the ISA/
Swedish Patent Office
Box 5055, S-102 42 STOCKHOLM
Facsimile No. +46 8 666 02 86

Date of mailing of the international search report

29 -07- 1993

Authorized officer

Mikael G:son Bergstrand
Telephone No. +46 8 782 25 00

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 93/00375

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	INFECTION AND IMMUNITY, 58(1990-05):5 William Kastern et al: "Protein L, a Bacterial Immunoglobulin-Binding Protein and Possible Virulence Determinant", page 1217 - page 1222; see especially fig. 4 and 5	1-2,8-14
Y	-----	3-14

INTERNATIONAL SEARCH REPORT
 Information on patent family members

02/07/93

International application No.

PCT/SE 93/00375

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A2- 0255497	03/02/88	JP-A- 63032372 US-A- 4876194	12/02/88 24/10/89
WO-A1- 8705631	24/09/87	DE-A- 3783191 EP-A,B- 0262192 SE-T3- 0262192	04/02/93 06/04/88